

AMENDMENTS TO THE CLAIMS

Claim 1 (withdrawn): A method of reducing the systemic release of radioactive decay intermediates upon administration of a radionuclide-emitting radionuclide to an individual, comprising the steps of:

incorporating said radionuclide into said large liposomes having a diameter sufficient to retain at least a majority of said radioactive decay intermediates; and

administering said large liposomes to said individual, wherein retention within said large liposomes of said radioactive decay intermediates by said radionuclide reduces the systemic release thereof.

Claim 2 (withdrawn): The method of claim 1, comprising:
entrapping said radionuclide within said smaller vesicles prior to incorporating said radionuclide contained therein into said larger liposome.

Claim 3 (withdrawn): The method of claim 2, comprising:
labeling said smaller liposomes with a specific targeting molecule.

Claim 4 (withdrawn): The method of claim 3, comprising the step of:
coating outer membrane surface of said large liposomes with molecules which preferentially associate with a specific target cell, wherein the specificity of said large liposomes to said target cell.

Claim 5 (withdrawn): The method of claim 4, wherein said target cell is a cancer cell, a virally infected cell, an autoimmune cell, or a cell of interest.

Claim 6 (withdrawn): The method of claim 4, wherein said molecules are antibodies, peptides, engineered molecules or fragments thereof.

Claim 7 (withdrawn): The method of claim 6, wherein said antibodies are Herceptin.

Claim 8 (withdrawn): The method of claim 1, further comprising the steps of:

preinjecting the individual with empty liposomes;
saturating the reticuloendothelial organs with said empty liposomes; and
spleen and liver uptake of said radioactive liposomes upon administration of said radioactive liposomes.

Claim 9 (withdrawn): The method of claim 1, wherein said large liposomes have a diameter of about 500 nm to about 1000 nm.

Claim 10 (withdrawn): The method of claim 1, wherein said large liposomes comprise molecules incorporated into or on the surface of said large liposomes.

Claim 11 (withdrawn): The method of claim 1, wherein said stabilizing molecules are polyethyleneglycol-linked lipids (PEG-lipids).

Claim 12 (withdrawn): The method of claim 1, wherein said stabilizing molecules further comprise an antibody, peptide, enzyme, or fragment thereof attached thereto.

Claim 13 (withdrawn): The method of claim 1, wherein said large liposomes comprise a stabilizing agent incorporated into or on the surface of said large liposomes in an aqueous phase with a high pH thereby further facilitating stabilization of said radioactive intermediates.

Claim 14 (withdrawn): The method of claim 1, wherein said stabilizing agent is a phosphate buffer, insoluble metal binding proteins, metal binding molecules or halogen binding molecules.

Claim 15 (withdrawn): The method of claim 1, wherein said large liposomes comprise additional molecules, said additional molecules being used for targeting with target cells or facilitating endocytosis by target cells.

Claim 16 (withdrawn): The method of claim 1, wherein said alpha particle emitting radionuclide is incorporated into the aqueous phase of said compound.

Claim 17 (withdrawn): The method of claim 1, wherein said alpha particle-emitting radionuclide is ^{225}Ac , ^{223}Ra , ^{213}Bi , or ^{212}Pb .

Claim 18 (withdrawn): The method of claim 1, wherein said alpha particle-emitting radionuclide is a daughter of a beta particle-emitting radionuclide, wherein said beta particle-emitting radionuclide is incorporated into the aqueous phase of said compound.

Claim 19 (withdrawn): The method of claim 1, wherein said beta particle-emitting radionuclide is ^{212}Pb .

Claim 20 (currently amended): A method of delivering a radionuclide to an individual for liposomal delivery of an alpha particle-emitting radionuclide with reduced systemic release of radioactive decay intermediates, comprising:

entrapping passively said radionuclide in said smaller liposomal vesicles;

incorporating said entrapped radionuclide into said larger liposomes of large liposomes, said liposomes having a diameter sufficient to retain a majority of the radioactive decay intermediates of said radionuclide;

polyethyleneglycol-linked lipids (PEGL) and phospholipids thereof;

and

a targeting agent attached to the PEGL, wherein said targeting agent is specific to the cells; and

delivering said radionuclide to the cells, wherein said targeting agents target the cells while retention within said large liposomes of said radioactive decay intermediates produced by said radionuclide reduces the systemic release of said intermediates.

Claim 21 (original): The method of claim 20, comprising the steps of: labeling said smaller liposomal vesicles with said radionuclide;

Claim 22 (original): The method of claim 20, comprising the steps of:

steps of:

preinjecting the individual with empty large liposomes;

Claim 32 (original): The method of claim 31, wherein said alpha particle-emitting radionuclide is a daughter of a beta particle-emitting radionuclide, wherein said beta particle-emitting radionuclide is entrapped within said liposomal vesicles.

Claim 33 (original): The method of claim 31, wherein said beta particle-emitting radionuclide is ^{225}Ac .

Claim 34 (withdrawn): A method of treating a cancer expressing HER-2/neu protein in an individual for liposomal delivery with reduced systemic release of radioactive decay intermediates of ^{225}Ac , comprising the steps of:

entrapping said ^{225}Ac within said liposomes;
incorporating said entrapped ^{225}Ac into said liposomes of large liposomes, said liposomes having a diameter of at least 100 nm, a majority of the radioactive decay intermediates of ^{225}Ac said liposomes;
polyethyleneglycol-linked lipids (PEG-lipids) incorporated into outer membranes thereof; and
Herceptin antibodies attached to the liposomes;
delivering said ^{225}Ac to the cancer cells, wherein Herceptin targets the HER-2/neu protein expressed on the cells while the large liposomes of said radioactive decay intermediates prevent their release, thus reduces the systemic release thereof.

Claim 35 (withdrawn): The method of claim 34, comprising:
labeling said smaller liposomal vesicles with a radioactive tracer;

Claim 36 (withdrawn): The method of claim 34, comprising the steps of:
preinjecting the individual with empty liposomes;
saturating the reticuloendothelial organs (spleen and liver uptake of said radionuclide upon injection).

Claim 37 (withdrawn): The method of claim 36 wherein said large liposomes have a diameter of about 500 nm to about 1000 nm.

Claim 38 (withdrawn): The method of claim 36 wherein said cancer cells comprise an ovarian carcinoma.

Claim 39 (withdrawn): The method of claim 36 wherein said large liposomes further comprise a stabilizing agent in an aqueous phase with a high pH thereby further facilitating the radioactive decay intermediates.

Claim 40 (withdrawn): The method of claim 36 wherein said stabilizing agent is a phosphate buffer, insoluble metal binding agent, metal-binding molecules or halogen binding molecules.

Claim 41 (withdrawn): The method of claim 36 wherein said large liposomes further comprise additional molecules, said additional molecules promoting membrane fusion with target cells or facilitating endocytosis by target cells.

Claim 42 (withdrawn): The method of claim 36 wherein said Ac-225 is chelated.

Claim 43 (withdrawn): An encapsulated radionuclide comprising:

said alpha particle emitting radionuclide;

small liposome vesicles encapsulating said alpha particle emitting radionuclide; and

a large liposome incorporating said small liposome vesicles, said large liposome having a diameter sufficient to retain at least a portion of said alpha particle emitting radionuclide intermediates, said alpha particle emitting radionuclide intermediates.

Claim 44 (withdrawn): The encapsulated radionuclide of claim 43 comprising:

labeling said smaller liposomal vesicles.

Claim 45 (withdrawn): The encapsulation of claim 43, wherein said alpha particle emitting radionuclide is ^{212}Pb , or ^{211}At .

Claim 46 (withdrawn): The encapsulation of claim 39, wherein said alpha particle-emitting radionuclide is ^{212}Pb , or ^{211}At , wherein said beta particle-emitting radionuclide is ^{212}Bi .

Claim 47 (withdrawn): The encapsulation of claim 46, wherein said beta particle-emitting radionuclide is ^{212}Bi .

Claim 48 (withdrawn): The encapsulation of claim 43, wherein said radionuclide associates with a membrane of said liposome or is incorporated into the aqueous compartment of said liposome as a chelation compound.

Claim 49 (withdrawn): The encapsulation of claim 43, wherein said large liposomes have a diameter of about 500 nm to about 1000 nm.

Claim 50 (withdrawn): The encapsulation of claim 43, wherein said large liposomes further comprise molecules that associate with a target cell, said molecules coating outer membrane of said large liposomes.

Claim 51 (withdrawn): The encapsulation of claim 50, wherein said molecules are antibodies, peptides, or proteins, or fragments thereof.

Claim 52 (withdrawn): The encapsulation of claim 50, wherein at least some of said antibodies are Herceptin.

Claim 53 (withdrawn): The encapsulated radiopharmaceutical of claim 50, wherein said target cell is a cancer cell, a virally infected cell, a stem cell, or an inflammatory cell.

Claim 54 (withdrawn): The encapsulated radiopharmaceutical of claim 43, wherein said large liposomes further comprise stabilizing molecules on their outer membranes to stabilize said large liposomes.

Claim 55 (withdrawn): The method of claim 43, wherein said stabilizing molecules further comprise an antibody, peptide, or a derivative or fragment thereof attached thereto.

Claim 56 (withdrawn): The encapsulated radiopharmaceutical of claim 54, wherein said stabilizing molecules are polyethers, polyesters, or phospholipids.

Claim 57 (withdrawn): The encapsulated radiopharmaceutical of claim 43, wherein said large liposomes comprise a stabilizing agent which is a polymer or have an aqueous phase with a high pH.

Claim 58 (withdrawn): The encapsulated radiopharmaceutical of claim 57, wherein said stabilizing agent is a phosphate buffer, a binding polymer, resin beads, metal-binding molecules or halogen compounds.

Claim 59 (withdrawn): The encapsulated radiopharmaceutical of claim 43, wherein said large liposomes comprise molecules that interact with a target cell or facilitating endocytosis by a target cell.